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Published in:
Rheumatology

DOI:
[10.1093/rheumatology/kex150](https://doi.org/10.1093/rheumatology/kex150)

Publication date:
2017

Document Version
Peer reviewed version

[Link to publication in Discovery Research Portal](#)

Citation for published version (APA):

Hui, M., Carr, A., Cameron, S., Davenport, G., Doherty, M., Forrester, H., Jenkins, W., Jordan, K. M., Mallen, C. D., MacDonald, T., Nuki, G., Pywell, A., Zhang, W., & Roddy, E. (2017). The British Society for Rheumatology Guideline for the Management of Gout. *Rheumatology*, 56(7), 1056-1059.
<https://doi.org/10.1093/rheumatology/kex150>

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British Society for Rheumatology and British Health Professionals in Rheumatology Guideline for the Management of Gout

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Short running title: BSR and BHPR Guideline for the Management of Gout

Scope and purpose of the guideline

Need for a revised management guideline

The British Society for Rheumatology/British Health Professionals in Rheumatology guideline for the management of gout was published in 2007¹. A revised and updated guideline is now required because of the availability of new pharmaceutical treatment options; recent increases in the incidence, prevalence and severity of gout²; continuing suboptimal management in both primary and secondary care^{2,3}; and better understanding of patient and provider barriers to effective care.^{4,5}

Objectives of the guideline

To offer revised and updated, concise, patient-focussed, evidence-based, expert recommendations for the management of gout in the UK.

Target Audience

To provide assistance to doctors and allied health professionals who treat and manage patients with gout in primary care and hospital practice.

Areas that the guideline does not cover

This guideline does not cover the diagnosis and investigation of gout.

This guideline has been reviewed and endorsed by the Royal College of General Practitioners (RCGP).

Key recommendations from this guideline

Management of Acute Attacks

- I. Educate patients to understand that attacks should be treated as soon as an attack occurs and ensure that patients are aware of the importance of continuing any established urate-lowering therapy during an attack. (Level of Evidence (LoE) IV, Strength of Recommendation (SOR) 90%)

- II. Affected joints should be rested, elevated and exposed in a cool environment. Bed-cages and ice-packs can be effective adjuncts to management. (LoE Ib (ice-packs), IV (other), SOR 89%)

- III. A non-steroidal anti-inflammatory drug (NSAID) at maximum dose or colchicine in doses of 500 micrograms bd-qds are the drugs of choice when there are no contraindications. Choice of first line agent will depend on patient preference, renal function and co-morbidities. Patients on NSAIDs or coxibs should be co-prescribed a gastro-protective agent. (LoE Ia, SOR 95%)

- IV. Joint aspiration and injection of a corticosteroid are highly effective in acute monoarticular gout and may be the treatment of choice in patients with acute illness and co-morbidity. A short course of oral corticosteroid or a single injection of an intra-muscular corticosteroid are alternatives in patients who are unable to tolerate NSAIDs/colchicine and in whom intra-articular injection is not feasible. Such systemic therapy is also

appropriate for oligo- or polyarticular attacks of gout. (LoE Ib (oral), III (intra-articular, intra-muscular), IV (oligo/polyarticular attacks), SOR 94%)

- V. In patients with acute gout where response to monotherapy is insufficient, combinations of treatment can be used. (LoE IV, SOR 80%)
- VI. Interleukin-1 inhibitors may be considered in patients who have previously not responded adequately to standard treatment of acute gout (although not approved by NICE). (LoE Ib (canakinumab, rilonacept), III (anakinra), SOR 61%)

Modification of lifestyle and risk factors

- VII. If diuretic drugs are being used to treat hypertension rather than heart failure, an alternative antihypertensive agent can be considered as long as blood pressure is controlled. (LoE IV, SOR 91%)
- VIII. All patients with gout should be given verbal and written information about: the causes and consequences of gout and hyperuricaemia; how to manage acute attacks; lifestyle advice about diet, alcohol consumption and obesity; and the rationale, aims and use of urate-lowering therapy to target urate levels. Management should be individualised and take into account co-morbidities and concurrent medications. Illness perceptions and potential barriers to care should be discussed. (LoE IIb, SOR 96%)
- IX. In overweight patients, dietary modification to achieve a gradual reduction in body weight and subsequent maintenance should be

encouraged. Diet and exercise should be discussed with all patients with gout, and a well-balanced diet low in fat and added sugars, and high in vegetables and fibre should be encouraged: sugar sweetened soft drinks containing fructose should be avoided; excessive intake of alcoholic drinks and high purine foods should be avoided; and inclusion of skimmed milk and/or low fat yoghurt, soy beans and vegetable sources of protein and cherries, in the diet should be encouraged. (LoE I (vitamin C and skimmed milk), III (others), SOR 92%)

- X. Patients with gout and a history of urolithiasis should be encouraged to drink >2litres of water daily and avoid dehydration. Alkalinisation of the urine with potassium citrate (60mEq/day) should be considered in recurrent stone formers (LoE IV, SOR 57%)
- XI. Cardiovascular risk factors and co-morbid conditions such as cigarette smoking, hypertension, diabetes mellitus, dyslipidaemia, obesity and renal disease should be screened for in all patients with gout, reviewed at least annually and managed appropriately. (LoE III, SOR 90%)

Optimal use of urate-lowering therapies

- XII. The option of urate-lowering therapy (ULT) should be explained to patients when the diagnosis is confirmed and they are being given information about gout. Patients should be fully involved in the decision as to when to commence ULT. The importance of taking ULT regularly and continually to prevent the return of gout attacks should be explained. Patients should be supported during the process of lowering their serum

uric acid levels as it can cause an increase in gout flares during this time.

(LoE Ib, SOR 94%)

- XIII. ULT should be discussed and offered to all patients who have a diagnosis of gout. ULT should particularly be advised in patients with: recurring attacks (≥ 2 attacks in 12 months); tophi; chronic gouty arthritis; joint damage; renal impairment (eGFR <60 ml/min); a history of urolithiasis; diuretic therapy use; and primary gout starting at a young age. (LoE Ia (attacks, tophi, chronic gouty arthritis, joint damage, renal impairment), III (urolithiasis), IV (diuretics, young age), SOR 95%)
- XIV. Commencement of ULT is best delayed until inflammation has settled as ULT is better discussed when the patient is not in pain. (LoE IV, SOR 94%)
- XV. The initial aim of ULT is to reduce and maintain the serum uric acid (sUA) level at or below a target level of 300 μ mol/L to prevent further urate crystal formation and to dissolve away existing crystals. The lower the sUA the greater the velocity of crystal elimination. After some years of successful treatment, when tophi have resolved and the patient remains free of symptoms, the dose of ULT can be adjusted to maintain the sUA at or below a less stringent target of 360 μ mol/l to avoid further crystal deposition and the possibility of adverse effects that may be associated with a very low sUA. (LoE III (sUA target <300 μ mol/L), -IV (subsequent dose adjustment to sUA $<360\mu$ mol/L), SOR 97%)
- XVI. Allopurinol is the recommended first-line ULT to consider. It should be started at a low dose (50-100mg daily) and the dose then increased in 100mg increments approximately every 4 weeks until the sUA target has

been achieved (maximum dose 900mg). In patients with renal impairment smaller increments (50mg) should be used and the maximum dose will be lower, but target urate levels should be the same. (LoE Ib (dose escalation), III (dose adjustment for renal function), SOR 97%)

- XVII. Febuxostat can be used as an alternative second line xanthine oxidase (XO) inhibitor for patients in whom allopurinol is not tolerated or whose renal impairment prevents allopurinol dose escalation sufficient to achieve the therapeutic target. Start with a dose of 80mg daily and, if necessary, increase after 4 weeks to 120mg daily, to achieve therapeutic target. (LoE Ia, SOR 90%)
- XVIII. Uricosuric agents can be used in patients who are resistant to, or intolerant of, XO-inhibitors. The preferred drugs are sulfinpyrazone (200-800 mg/day) or probenecid (500-2000mg/day) in patients with normal or mildly impaired renal function, or benzbromarone (50-200mg/day) in patients with mild-moderate renal insufficiency. (LoE Ia, SOR 92%)
- XIX. Losartan and fenofibrate should not be used as a primary ULT but where treatment for hypertension or dyslipidaemia, respectively, are required, they may be considered as they have a weak uricosuric effect. Vitamin C supplements (500mg – 1500mg daily) also have a weak uricosuric effect. (LoE III, SOR 89%)
- XX. A uricosuric agent can be used in combination with a xanthine oxidase inhibitor in patients who do not achieve a therapeutic serum urate target with optimal doses of monotherapy. (LoE III, SOR 88%)

XXI. Colchicine 500micrograms bd or od should be considered as prophylaxis against acute attacks resulting from initiation or up-titration of any ULT and continued for up to 6 months. In patients who cannot tolerate colchicine, a low-dose NSAID or Coxib, with gastroprotection, can be used as an alternative providing there are no contraindications. (LoE Ib, SOR 86%)

The full guideline, available at *Rheumatology* online, contains specific recommendations for management of gout in special groups: patients with renal sufficiency, severe refractory tophaceous gout, and in pregnancy. Figure 1 illustrates the suggested care pathway.

Conflicts of interest

G.D. has received honoraria for *ad hoc* advisory board meetings relating to gout from AstraZeneca. M.D. has received honoraria for *ad hoc* advisory boards relating to osteoarthritis and gout from Ardea Biosciences, AstraZeneca, Nordic Biosciences and Roche; AstraZeneca are funding a Nottingham University investigator-led non-drug study on gout. T.M. leads a university-sponsored clinical trial (Febuxostat v. Allopurinol Streamlined safety Trial (FAST)) funded by Menarini. G.N. has undertaken paid consultancy for Savient, is a member of the Independent Disease Monitoring Committee for trials of lesinurad (Ardea/AstraZeneca), and has received honoraria for advisory boards from Menarini and research funding from Menarini for the FAST trial. W.Z. has received honoraria or speaker fees from Daiichi Sankyo, AstraZeneca, Biobarica and Hisun. All other authors have declared no conflicts of interest.

Funding statement

No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this manuscript.

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Figure 1 Algorithm for the management of gout